

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and the following commentary.

I. Status of the Claims

Claims 2-12 were previously cancelled. Claims 25-29 are cancelled in this response, without prejudice or disclaimer. Claim 1 has been amended to set forth the subject matter more clearly. Because no new matter is introduced, Applicant respectfully requests entry of this amendment. Upon entry, claims 1, and 13-24 will be pending.

II. Double Patenting Rejection

The Examiner alleges that claims 1, 13-15, 20, 21, 25, 26 and 28 conflict with claims 1-5 and 7-13 of the copending Application No. 10/594,898. Applicants respectfully traverse the rejection.

Applicants submit that the claims in the '898 application do not conflict with the present claims. Specifically, claim 1 of the '898 application prescribes that "the quinone dye is not formed in the first step" of the method. By contrast, the claimed method requires that the first step of the reaction generates a compound, such as a quinone dye, and measures the amount of the compound. Accordingly, the double patenting rejection should be withdrawn because conflicting claims do not exist in the copending application.

III. Rejection of Claims under 35 U.S.C. § 102(b)

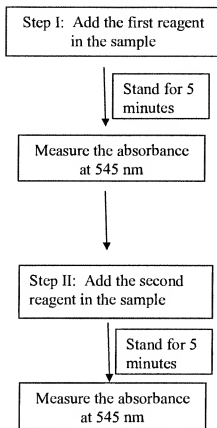
A. U.S. Patent No. 6,333,166 B1 to Nakamura

The Examiner rejected claims 1, 13, and 20-22 for alleged anticipation by U.S. Patent No. 6,333,166 B1 to Nakamura *et al.* Applicant respectfully traverses the rejection.

The principal of the claimed invention is distinguished from Nakamura, which results in the difference in the value measured by each method. Specifically, the method prescribed by claim 1 involves two steps and the use of two reagents. In the first step, the first reagent acts on the cholesterol in lipoproteins other than low density lipoprotein (LDL) to generate a compound, and in the second step, the second reagent acts on the remaining LDL to generate additional amount of the compound, such that the value from step (i) represents the amount of the cholesterol in lipoproteins other than LDL, the value from step (ii) represents the amount of total cholesterol in said sample, and the difference in values from step (i) and step (ii) represents the amount of cholesterol in low density lipoprotein.

By contrast, Nakamura's methodology relates to the discovery of "a specific surfactant which *dissolves lipoproteins accelerates reaction of HDL cholesterol and VLDL cholesterol and remarkably retards reaction of LDL cholesterol*; that *reaction of HDL cholesterol and VLDL cholesterol are terminated prior to reaction of LDL cholesterol*; and that LDL cholesterol can be measured quantitatively and fractionally by appropriate selection of a point of measurement" (column 2, lines 39-46; emphasis added). Moreover, Nakamura states that the function of the surfactant is to "induce preferential reactions of cholesterol in high density- and very low density-lipoproteins among lipoproteins, and subsequently determining the amount of cholesterol which reacts thereafter." Column 2, lines 54-58. In brief, the prior-art methodology entails an elimination or "dissolve[ing]" of HDL and VLDL, followed by a measurement of the amount of the remaining LDL.

This is evident from the disclosure of Example 2, column 5, lines 31-54, which the Examiner mentions in his rejection. A flow chart below summarizes the protocol of the prior art:



The prior art teaches that the first reagent contains Emulgen B66, cholesterol esterase, cholesterol oxidase, peroxidase and 4-aminoantipyrine, and that the second reagent contains Triton X-100 and N,N-dimethyl-m-toluidine (*supra*). In step I of Nakamura's method, dissolving of HDL and VLDL is accelerated while reaction of LDL is remarkably retarded in the presence of Emulgen B66. Also, step I does not generate any colored compound detectable at 545 nm, due to the absence of N,N-dimethyl-m-toluidine. Therefore, the measurement following step I only generates the baseline reading of the reaction mix, rather than the amount of cholesterol in lipoproteins other than low density lipoprotein, as recited in claim 1.

In addition, HDL and VLDL are dissolved in step I of the prior-art method, and the condensation reaction between 4-aminoantipyrine and N-dimethyl-m-toluidine, which is only introduced in step II, results in colored quinone. Accordingly, the value obtained following step II represents the amount of LDL in the sample rather than the total cholesterol, as the Examiner contends.

It is apparent, therefore, that the prior-art method neither teaches step (i) of the claimed method nor provides a measurement of the total cholesterol. The Nakamura patent therefore does not anticipate the claimed invention.

B. U.S. Patent No. 6,194,164 B1

The Examiner rejected claims 25, and 27-29 for alleged anticipation by U.S. Patent No. 6,194,164 B1 to Matsui *et al.* Without acquiescing to the stated rationale of the rejection, Applicant has cancelled claims 25 and 27-29, mooted the rejection.

IV. Rejection of Claims under 35 U.S.C. § 103(a)

A. U.S. Patent No. 6,194,164 B1

The Examiner rejected claims 25-29 for alleged obviousness over U.S. Patent No. 6,194,164 B1 to Matsui *et al.* Without acquiescing to the Examiner's stated rationale, Applicant has obviated the rejection by cancelling claims 25-29.

B. U.S. Patent Nos. 6,333,166 B1 and 6,194,164 B1

The Examiner rejected claims 1, 13-16 and 19-22 for alleged obviousness over U.S. Patent No. 6,333,166 B1 to Nakamura *et al.* in view of U.S. Patent No. 6,194,164 B1 to Matsui *et al.* Applicant respectfully traverses the rejection.

As discussed above, Nakamura's methodology does not teach step (i) of the claimed method. Moreover, contrary to the Examiner's contention, Nakamura does not determine the total cholesterol. Action, page 7, line 4. Similarly, Matsui describes "erasing cholesterol in high density lipoprotein, very low density lipoprotein and chylomicron...and...[then] quantifying cholesterol remaining in the test sample" (abstract). Therefore, Nakamura and Matsui in combination do not teach a method that is capable of measuring *the total cholesterol* as well as the LDL. Accordingly, the withdrawal of the obviousness rejection is warranted.

C. U.S. Patent Nos. 6,333,166 B1 and 6,794,157 B1

The Examiner rejected claims 1, 13, 17, 18, and 20-22 for alleged obviousness over U.S. Patent No. 6,333,166 B1 to Nakamura *et al.* in view of U.S. Patent No. 6,794,157 B1 to Sugiuchi. Applicant respectfully traverses the rejection.

The teaching of Nakamura is discussed above. The Examiner appears to cite Sugiuchi for the alleged teaching of the use of cholesterol dehydrogenase or NAD. Nevertheless, Sugiuchi does not compensate for the deficiency of the primary reference. Therefore, Applicant requests withdrawal of the rejection.

D. U.S. Patent No. 6,333,166 B1 and U.S. Patent Application Publication No. 2003/0129681 A1

The Examiner rejected claims 1, 13, and 20-24 for alleged obviousness over U.S. Patent No. 6,333,166 B1 to Nakamura *et al.* in view of U.S. Patent Application Publication No. 2003/0129681 A1 by Kishi *et al.* Applicant respectfully traverses the rejection.

By the same token, Kishi is cited for the alleged teaching of the use of albumin and lipoprotein lipase. Because Kishi also fails to remedy the deficiency of the primary reference, the combined teachings of Nakamura and Kishi do not render the claimed invention obvious.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account.

If any extension is needed for timely acceptance of submitted papers, Applicant hereby petitions for such extension under 37 CFR §1.136 and authorizes payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

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